Alexion Receives FDA Approval for New Advanced Formulation of ULTOMIRIS® (ravulizumab-cwvz) with Significantly Reduced Infusion Time

October 12, 2020

– New 100 mg/mL formulation will reduce infusion time by approximately 60 percent, lessening the burden on patients –

– ULTOMIRIS is approved for the treatment of paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS) –

BOSTON--(BUSINESS WIRE)--Oct. 12, 2020-- Alexion Pharmaceuticals, Inc. (NASDAQ:ALXN) today announced the U.S. Food and Drug Administration (FDA) has approved ULTOMIRIS® (ravulizumab-cwvz) 100 mg/mL formulation for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH) and for atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy for adult and pediatric (one month of age and older) patients. ULTOMIRIS 100 mg/mL is an advancement in the treatment experience for patients with aHUS and PNH, as it reduces average annual infusion times by approximately 60 percent compared to ULTOMIRIS 10 mg/mL while delivering comparable safety and efficacy. With ULTOMIRIS 100 mg/mL, most patients will spend six hours or less a year receiving treatment.

This press release features multimedia. View the full release here: https://www.businesswire.com/news/home/20201012005090/en/

Image of ULTOMIRIS® (ravulizumab-cwvz) 100 mg/mL vials (3 mL and 11mL) (Photo: Business Wire)

"We have seen the significant clinical benefits ULTOMIRIS has demonstrated for patients, through its complete C5 inhibition and sustained efficacy," said Jamile Shammo, M.D., FASCP, FACP, Professor of Medicine and Pathology, Department of Internal Medicine, Rush University Medical Center. "Based on the scientific evidence presented, the advanced formulation demonstrated comparable safety and efficacy to the original formulation, with the additional benefit of significantly shorter infusion times. This reduced treatment burden is important to consider for patients, as it has the potential to make a meaningful difference in their lives."

PNH is a blood disorder characterized by complement-mediated destruction of the red blood cells that can cause a wide range of debilitating symptoms and complications, including thrombosis, which can occur throughout the body, and result in organ damage and premature death. Atypical HUS can cause progressive injury to vital organs, primarily the kidneys, via damage to the walls of blood vessels and blood clots. Affecting both adults and children, atypical HUS patients can present in critical condition, often requiring supportive care, including dialysis, in an intensive care unit. The prognosis of both aHUS and PNH can be poor in many cases, so a timely and accurate diagnosis—in addition to appropriate treatment—is critical to improving patient outcomes.

"ULTOMIRIS is the market leader for the treatment of PNH and is emerging as the standard of care for the treatment of aHUS," said John Orloff, M.D., Executive Vice President and Head of Research and Development at Alexion. "The approval of ULTOMIRIS 100 mg/mL represents the next step in advancing patient care for the PNH and aHUS communities, as it reduces infusion times for patients and decreases the number of vials that need to be stored and prepared for the majority of patients' infusions, allowing healthcare providers more time to focus on the patient. With ULTOMIRIS 100 mg/mL, most patients will spend six hours or less each year receiving treatment, giving them more time to do what they enjoy, which we believe will provide a meaningful benefit to their quality of life."

Alexion plans to make ULTOMIRIS 100 mg/mL available within a few days and has comprehensive training plans to educate all stakeholders about the new formulation. ULTOMIRIS 10 mg/mL will continue to be available until mid-2021, at which time Alexion will remove ULTOMIRIS 10 mg/mL from the market, as communicated to the FDA. The transition period is intended to provide a seamless conversion to the new formulation without interruption to patients' infusion schedules.

Regulatory filings for marketing authorizations of the 100 mg/mL formulation of ULTOMIRIS are under review with regulators in the European Union (EU) and Japan. The Committee for Medicinal Products for Human Use (CHMP) has recently adopted a positive opinion, recommending marketing authorization of ULTOMIRIS 100 mg/mL in the European Union, and we anticipate receiving a decision from the European Commission in November.

Alexion continues to innovate with ULTOMIRIS, with the goal of improving the patient experience. We plan to submit regulatory filings in the U.S. and EU in the third quarter of 2021 for an ULTOMIRIS subcutaneous formulation and device combination for PNH and aHUS that can be self-administered at home, pending completion of the ongoing Phase 3 study and collection of 12-month safety data. In addition, the collective ULTOMIRIS clinical development programs present an opportunity to expand the treated patient populations across hematology, nephrology, neurology and for the treatment of severe COVID-19, with seven Phase 3 programs that are ongoing or have planned clinical trial initiations in 2020.

About Paroxysmal Nocturnal Hemoglobinuria (PNH)

PNH is a serious ultra-rare blood disorder with devastating consequences. It is characterized by the destruction of red blood cells, which is also referred to as hemolysis. PNH occurs when the complement system—a part of the body's immune system—over-responds, leading the body to attack its own red blood cells. PNH often goes unrecognized, with delays in diagnosis from one to more than five years. Patients with PNH may experience a range of symptoms, such as fatigue, difficulty swallowing, shortness of breath, abdominal pain, erectile dysfunction, dark-colored urine and anemia. The most devastating consequence of chronic hemolysis is the formation of blood clots, which can occur in blood vessels throughout the body, damage vital organs, and potentially lead to premature death. PNH can strike men and women of all races, backgrounds and ages without warning, with an average age of onset in the early 30s.

About Atypical Hemolytic Uremic Syndrome (aHUS)

aHUS is an ultra-rare disease that can cause progressive injury to vital organs, primarily the kidneys, via damage to the walls of blood vessels and blood clots. aHUS occurs when the complement system—a part of the body's immune system—over-responds, leading the body to attack its own healthy cells. aHUS can cause sudden organ failure or a slow loss of function over time—potentially resulting in the need for a transplant, and in some cases, death. aHUS affects both adults and children, and many patients present in critical condition, often requiring supportive care, including dialysis, in an intensive care unit. The prognosis of aHUS can be poor in many cases, so a timely and accurate diagnosis—in addition to treatment—is critical to improving patient outcomes. Available tests can help distinguish aHUS from other hemolytic diseases with similar symptoms.

About ULTOMIRIS®

ULTOMIRIS® (ravulizumab-cwvz) is the first and only long-acting C5 complement inhibitor. The medication works by inhibiting the C5 protein in the terminal complement cascade, a part of the body's immune system. When activated in an uncontrolled manner, the complement cascade over-responds, leading the body to attack its own healthy cells. ULTOMIRIS is administered intravenously every eight weeks or, for pediatric patients less than 20 kg, every four weeks, following a loading dose. ULTOMIRIS is approved in the United States (U.S.), European Union (EU) and Japan as a treatment for adults with paroxysmal nocturnal hemoglobinuria (PNH). It is also approved in the U.S. and Japan for atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy (TMA) in adult and pediatric (one month of age and older) patients, as well as in the EU for the treatment of adults and children with a body weight of at least 10 kg with aHUS. To learn more about the regulatory status of ULTOMIRIS in the countries that we serve, please visit www.alexion.com.

INDICATIONS & IMPORTANT SAFETY INFORMATION for ULTOMIRIS® (ravulizumab-cwvz)

INDICATIONS

What is ULTOMIRIS?

ULTOMIRIS is a prescription medicine used to treat:

- adults with a disease called Paroxysmal Nocturnal Hemoglobinuria (PNH).
- adults and children 1 month of age and older with a disease called atypical Hemolytic Uremic Syndrome (aHUS). ULTOMIRIS is not used in treating people with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

It is not known if ULTOMIRIS is safe and effective in children with PNH.

It is not known if ULTOMIRIS is safe and effective in children younger than 1 month of age.

IMPORTANT SAFETY INFORMATION

What is the most important information I should know about ULTOMIRIS?

ULTOMIRIS is a medicine that affects your immune system and can lower the ability of your immune system to fight infections.

- ULTOMIRIS increases your chance of getting serious and life-threatening meningococcal infections that may quickly become life-threatening and cause death if not recognized and treated early.

1. You must receive meningococcal vaccines at least 2 weeks before your first dose of ULTOMIRIS if you are not vaccinated.
2. If your doctor decided that urgent treatment with ULTOMIRIS is needed, you should receive meningococcal vaccination as soon as possible.
3. If you have not been vaccinated and ULTOMIRIS therapy must be initiated immediately, you should also receive 2 weeks of antibiotics with your vaccinations.
4. If you had a meningococcal vaccine in the past, you might need additional vaccination. Your doctor will decide if you need additional vaccination.

5. Meningococcal vaccines reduce but do not prevent all meningococcal infections. Call your doctor or get emergency medical care right away if you get any of these signs and symptoms of a meningococcal infection: headache with nausea or vomiting, headache and fever, headache with a stiff neck or stiff back, fever, fever and a rash, confusion, muscle aches with flu-like symptoms and eyes sensitive to light.

Your doctor will give you a Patient Safety Card about the risk of meningococcal infection. Carry it with you at all times during treatment and for 8 months after your last ULTOMIRIS dose. It is important to show this card to any doctor or nurse to help them diagnose and treat you quickly.

ULTOMIRIS is only available through a program called the ULTOMIRIS REMS. Before you can receive ULTOMIRIS, your doctor must: enroll in the ULTOMIRIS REMS program; counsel you about the risk of meningococcal infection; give you information and a **Patient Safety Card** about the symptoms and your risk of meningococcal infection (as discussed above); and make sure that you are vaccinated with a meningococcal vaccine, and if needed, get revaccinated with the meningococcal vaccine. Ask your doctor if you are not sure if you need to be revaccinated.

ULTOMIRIS may also increase the risk of other types of serious infections. Make sure your child receives vaccinations against *Streptococcus pneumoniae* and *Haemophilis influenzae* type b (Hib) if treated with ULTOMIRIS. Call your doctor right away if you have any new signs or symptoms of infection.

Who should not receive ULTOMIRIS?

Do not receive ULTOMIRIS if you have a meningococcal infection or have not been vaccinated against meningococcal infection unless your doctor decides that urgent treatment with ULTOMIRIS is needed.

Before you receive ULTOMIRIS, tell your doctor about all of your medical conditions, including if you: have an infection or fever, are pregnant or plan to become pregnant, and are breastfeeding or plan to breastfeed. It is not known if ULTOMIRIS will harm your unborn baby or if it passes into your breast milk. You should not breastfeed during treatment and for 8 months after your final dose of ULTOMIRIS.

Tell your doctor about all the vaccines you receive and medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements which could affect your treatment.

If you have PNH and you stop receiving ULTOMIRIS, your doctor will need to monitor you closely for at least 16 weeks after you stop ULTOMIRIS. Stopping ULTOMIRIS may cause breakdown of your red blood cells due to PNH. Symptoms or problems that can happen due to red blood cell breakdown include: drop in your red blood cell count**,** tiredness**,** blood in your urine**,** stomach-area (abdomen) pain**,** shortness of breath**,** blood clots**,** trouble swallowing, and erectile dysfunction (ED) in males.

If you have aHUS, your doctor will need to monitor you closely for at least 12 months after stopping treatment for signs of worsening aHUS or problems related to a type of abnormal clotting and breakdown of your red blood cells called thrombotic microangiopathy (TMA). Symptoms or problems that can happen with TMA may include: confusion or loss of consciousness, seizures, chest pain (angina), difficulty breathing and blood clots or stroke.

What are the possible side effects of ULTOMIRIS?

ULTOMIRIS can cause serious side effects including infusion-related reactions. Symptoms of an infusion-related reaction with ULTOMIRIS may include lower back pain, pain with the infusion, feeling faint or discomfort in your arms or legs. Tell your doctor or nurse right away if you develop these symptoms, or any other symptoms during your ULTOMIRIS infusion that may mean you are having a serious infusion reaction, including: chest pain, trouble breathing or shortness of breath, swelling of your face, tongue, or throat, and feel faint or pass out.

The most common side effects of ULTOMIRIS in people treated for PNH are upper respiratory infection and headache.

The most common side effects of ULTOMIRIS in people with aHUS are upper respiratory infection, diarrhea, nausea, vomiting, headache, high blood pressure and fever.

Tell your doctor about any side effect that bothers you or that does not go away. These are not all the possible side effects of ULTOMIRIS. For more information, ask your doctor or pharmacist. Call your doctor right away if you miss an ULTOMIRIS infusion or for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

Please see the accompanying full Prescribing Information and Medication Guide for ULTOMIRIS, including Boxed WARNING regarding serious and life-threatening meningococcal infections/sepsis.

About Alexion

Alexion is a global biopharmaceutical company focused on serving patients and families affected by rare diseases and devastating conditions through the discovery, development and commercialization of life-changing medicines. As a leader in rare diseases for more than 25 years, Alexion has developed and commercializes two approved complement inhibitors to treat patients with paroxysmal nocturnal hemoglobinuria (PNH) and atypical hemolytic uremic syndrome (aHUS), as well as the first and only approved complement inhibitor to treat anti-acetylcholine receptor (AchR) antibody-positive generalized myasthenia gravis (gMG) and neuromyelitis optica spectrum disorder (NMOSD). Alexion also has two highly innovative enzyme replacement therapies for patients with life-threatening and ultra-rare metabolic disorders, hypophosphatasia (HPP) and lysosomal acid lipase deficiency (LAL-D) as well as the first and only approved Factor Xa inhibitor reversal agent. In addition, the company is developing several mid-to-late-stage therapies, including a copper-binding agent for Wilson disease, an anti-neonatal Fc receptor (FcRn) antibody for rare Immunoglobulin G (IgG)-mediated diseases and an oral Factor D inhibitor as well as several early-stage therapies, including one for light chain (AL) amyloidosis, a second oral Factor D inhibitor and a third complement inhibitor. Alexion focuses its research efforts on novel molecules and targets in the complement cascade and its development efforts on the core therapeutic areas of hematology, nephrology, neurology, metabolic disorders and cardiology. Headquartered in Boston, Massachusetts, Alexion has offices around the globe and serves patients in more than 50 countries. This press release and further information about Alexion can be found at: www.alexion.com.

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For patient or advocacy inquiries please contact *patientadvocacy@alexion.com*.

Forward-Looking Statement

This press release contains forward-looking statements that involve risks and uncertainties relating to future events and the future performance of Alexion, including statements related to: the safety, efficacy and benefits of the 100 mg/mL ULTOMIRIS formulation as a treatment for PNH and aHUS; the ability of the ULTOMIRIS 100 mg/mL formulation to reduce infusion time as compared to the 10mg/mL formulation of ULTOMIRIS by approximately 60% with comparable safety and efficacy; the potential for shorter infusion times will make a meaningful difference in patient lives; ULTOMIRIS is becoming the standard of care for patients with aHUS; the shorter infusion times for the 100mg/mL ULTOMIRIS formulation will result in patients spending six hours or less per year receiving treatment; the approval of ULTOMIRIS 100 mg/mL represents the next step in advancing patient care for the PNH and aHUS communities; ULTOMIRIS 100 mg/mL reduces infusion times for patients and decreases the number of vials that need to be stored and prepared for the majority of patients' infusions, allowing healthcare providers more time to focus on the patient; Alexion's plans to make ULTOMIRIS 100 mg/mL available to patients and its training plans to educate stakeholders about the new formulation; . Alexion's plans with respect to the availability of ULTOMIRIS 10 mg/mL formulation; plans for transitioning patients to the 100 mg/mL formulation; Alexion expects a marketing approval decision from the European Commission on the ULTOMIRIS 100 mg/mL formulation in November; our plans to submit regulatory filings in the U.S. and EU in the third quarter of 2021 for an ULTOMIRIS subcutaneous formulation and device combination for PNH and aHUS that can be self-administered at home; completion of ongoing Phase 3 study and collection of 12-month safety data; that the collective ULTOMIRIS clinical development programs present an opportunity to expand the treated patient populations across hematology, nephrology, neurology and for the treatment of severe COVID-19; and planned clinical trial initiations in 2020. Forward-looking statements are subject to factors that may cause Alexion's results and plans to differ materially from those expected by these forward looking statements, including for example: the anticipated safety profile and the benefits of the ULTOMIRIS 100 mg/mL formulation may not be realized (and the results of the clinical trials may not be indicative of future results); results of clinical trials may not be sufficient to satisfy regulatory authorities; results in clinical trials may not be indicative of results from later stage or larger clinical trials (or in broader patient populations); the possibility that results of clinical trials are not predictive of safety and efficacy and potency of our products (or we fail to adequately operate or manage our clinical trials) which could cause us to discontinue sales of the product (or halt trials, delay or prevent us from making regulatory approval filings or result in denial of approval of our product candidates); the severity of the impact of the COVID-19 pandemic on Alexion's business, including on commercial and clinical development programs; unexpected delays in clinical trials; unexpected concerns regarding products and product candidates that may arise from additional data or analysis obtained during clinical trials or obtained once used by patients following product approval; future product improvements may not be realized due to expense or feasibility or other factors; delays (expected or unexpected) in the time it takes regulatory agencies to review and make determinations on applications for the marketing approval of our products; inability to timely submit (or failure to submit) future applications for regulatory approval for our products and product candidates; inability to timely initiate (or failure to initiate) and complete future clinical trials due to safety issues, IRB decisions, CMC-related issues, expense or unfavorable results from earlier trials (among other reasons); our dependence on sales from our principal product (SOLIRIS); future competition from biosimilars and novel products; decisions of regulatory authorities regarding the adequacy of our research, marketing approval or material limitations on the marketing of our products; delays or failure of product candidates to obtain regulatory approval; delays or the inability to launch product candidates due to regulatory restrictions, anticipated expense or other matters; interruptions or failures in the manufacture and supply of our products and our product candidates; failure to satisfactorily address matters raised by regulatory agencies regarding our products and product candidates; uncertainty of long-term success in developing, licensing or acquiring other product candidates or additional indications for existing products; inability to complete acquisitions or grow the product pipeline through acquisitions (including due to failure to obtain antitrust approvals); the possibility that current rates of adoption of our products are not sustained; the adequacy of our pharmacovigilance and drug safety reporting processes; failure to protect and enforce our data, intellectual property and proprietary rights and the risks and uncertainties relating to intellectual property claims, lawsuits and challenges against us (including intellectual property lawsuits relating to ULTOMIRIS brought by third parties); the risk that third party payors (including governmental agencies) will not reimburse or continue to reimburse for the use of our products at acceptable rates or at all; failure to realize the benefits and potential of investments, collaborations, licenses and acquisitions; the possibility that expected tax benefits will not be realized; potential declines in sovereign credit ratings or sovereign defaults in countries where we sell our products; delay of collection or reduction in reimbursement due to adverse economic conditions or changes in government and private insurer regulations and approaches to reimbursement; adverse impacts on our supply chain, clinical trials, manufacturing operations, financial results, liquidity, hospitals, pharmacies and health care systems from natural disasters and global pandemics, including COVID-19; uncertainties surrounding legal proceedings, company investigations and government investigations; the risk that estimates regarding the number of patients with PNH, aHUS, gMG, NMOSD, HPP and LAL-D and other indications we are pursuing (as well as patients requiring a Factor Xa inhibitor reversal agent) are inaccurate; the risks of changing foreign exchange rates; risks relating to the potential effects of the Company's restructuring; risks related to the acquisitions of Portola Pharmaceuticals, Achillion and other companies and co-development efforts; and a variety of other risks set forth from time to time in Alexion's filings with the SEC, including but not limited to the risks discussed in Alexion's Quarterly Report on Form 10-Q for the period ended June 30, 2020 and in our other filings with the SEC. Alexion disclaims any obligation to update any of these forward-looking statements to reflect events or circumstances after the date hereof, except when a duty arises under law.

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